33IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEBRASKA

JAN VALLEJO, Individually and As Personal Representative of Steve Vallejo;

Plaintiff,

vs.

AMGEN, INC., WYETH, INC., AND PFIZER, INC.,

Defendants.

8:14CV50

ORDER

BACKGROUND

1. Factual Background

Plaintiff's complaint alleges Steve Vallejo ingested the prescription drug, Enbrel® (etanercept), which caused him to suffer from myelodysplastic syndrome ("MDS"), resulting in his death. Defendants assert there is no evidence that using Enbrel® causes MDS.

Enbrel® is an injectable prescription biologic product that "neutralizes" a tumor necrosis factor ("TNF") blocker, a protein made by the body's immune system. Enbrel® was first approved by the United States Food and Drug Administration ("FDA") in November 1998 for the treatment of rheumatoid arthritis. Since its initial approval in 1998, Enbrel® has been approved for treating a variety of health issues.

Plaintiff's husband, the Decedent, was prescribed Enbrel® for psoriasis and developed MDS. MDS is a hematological disorder characterized by the bone marrow's inability to produce a sufficient number of healthy erythrocytes (red blood cells), leukocytes (white blood cells including neutrophils, lymphocytes, monocytes, eosinophils, and basophils), and platelets. MDS represents of a heterogeneous group of related clonal

disorders affecting the formation and production of these cells (hematopoiesis) and may progress to anemia, leukemia, thrombocytopenia, pancytopenia, or severe marrow failure.

2. Procedural Background

On May 5, 2015, the court ordered phased discovery, the first phase focusing on general medical causation; that is, whether using Enbrel® can cause MDS. (Filing No. 55). Shortly thereafter, the parties requested a planning conference with the undersigned magistrate judge. During this conference, the parties discussed their views on the appropriate scope of discovery for the first phase and the court ordered that the parties brief the issue for decision on whether the scope of discovery should be limited. (Filing No. 57).

During a scheduling conference that followed, the parties continued to argue over the scope of discovery on the issue of causation. Accordingly, the court scheduled a hearing to discuss any unresolved discovery issues. The parties were ordered to file a joint outline of the discovery issues and their respective positions prior to the hearing. (Filing No. 69). The parties were unable to reach agreements and instead provided separate lists. The lists included the plaintiff's 66 discovery requests. On December 9, 2015, the court held a hearing on the record. On the court's own motion, the undersigned ordered the parties to provide the court with supplemental briefing outlining Defendant's potential burden and examining proportionality.

3. Demands and Offers to Date

At the December 9th hearing, Plaintiff's expert, Dr. Levesque testified that the following materials were relevant to her determination of causation. She requested:

- All available information for the MedWatch adverse event reports for MDS and all of its related symptomology as provided in the MedDRA SMQ for MDS – including the medical records for people associated with adverse events;
- Information from foreign sources;
- All preclinical data;

- All information from human studies (including phases 1, 2, & 3);
- Any study but particularly observational studies exploring the association between Enbrel® and all symptoms related to MDS;
- Information for other TNF blockers; and
- Enbrel® studies, regardless of the indication for which Enbrel® was used in this case.

As of the filing of this order, Defendants have offered to provide the following:

- MedWatch reports for adverse events for MDS which will include every adverse event report of MDS in any clinical trial;
- Any case report of MDS that has come out in any clinical trial using a MedWatch form;
- Every report that mentions or is for MDS from any country, source, clinical trial, or post marketing experience that is listed in Defendants' global safety database;
- The original Biologic License Application ("BLA") from 1998, including the index, the non-clinical pharmacology and toxicology sections, the human pharmacokinetics and bioavailability sections, the clinical section and the statistical section;
- Case report forms;
- The investigator brochure;
- The deposition of Ms. Jan Isles, the global safety officer for Enbrel®.

During the December 9th hearing, the court asked Plaintiff's counsel numerous times what the expert needed to formulate an opinion on whether a causal relationship exists between taking Enbrel® and MDS. Plaintiff's expert, Dr. Levesque, testified during the hearing that she needed everything the plaintiff originally requested;[1] that is, every document the defendants or any of its predecessors have or can access for any person who ingested

[1] The court notes that during the hearing, the plaintiff's expert testified that for her causation determination, she needed "the evidence [she was] provided for other cases [she has] worked on." (Filing No. 81 at CM/ECF p. 81). The court then directly asked whether, in other cases, she is normally provided with "every single clinical trial that has been done with a drug, whether it's a drug related to particular disease or disorder or not[.]" To which Dr. Levesque responded "Yes." However, later in the hearing, when defense counsel requested a list of cases in which Dr. Levesque has been involved, plaintiff's counsel stated Dr. Levesque has "never testified before."

Enbrel® and reported a symptom or impact on that person's red blood cells, white blood cells, platelets, or any precursor cells for these blood cell lines.

After considering Plaintiff's demands and that of her expert, the court finds the expert's testimony was not entirely credible, and her demands are unreasonable. This expert's testimony did not assist the court in determining whether Plaintiff's need for the requested information was proportional to the burden imposed on the defendants in responding to Plaintiff's discovery.[2]

"Enbrel® has been on the market since 1998, and has been prescribed to over 900,000 patients in the United States alone. It has been evaluated in nearly 200 different clinical studies for over 20 years, with over 25,000 global study patients at clinical sites around the world being observed for more than 34,000 patient-years of therapy across all indications. Defendants allege that producing all the information Plaintiff requests would cost millions of dollars. (Filing No. 70 at CM/ECF p. 11). Counsel for the defense also states that the only distinction between what Defendants have offered to provide and what Dr. Levesque requested in the hearing, is that the defendants are willing to produce information as to Enbrel® and a diagnosis of "MDS," while Plaintiff requests all information pertaining to a diagnosis of MDS and any reported symptom associated with MDS.

ANALYSIS

Rule 26(b) governs discovery and limits the scope of discovery to

> any nonprivileged matter that is relevant to any party's claim or defense and proportional to the needs of the case, considering the importance of the issues at stake in the action, the amount in controversy, the parties' relative access to relevant information, the parties' resources, the importance of the discovery in resolving the issues, and whether the burden or expense of the proposed

[2] Plaintiff's counsel indicated that the testifying expert would not actually be reviewing the discovery: She would look at the synthesis of the information prepared by Plaintiff's reviewing experts.

> discovery outweighs its likely benefit. Information within this scope of discovery need not be admissible in evidence to be discoverable.

Fed. R. Civ. P. 26(b)(1). Courts should examine each case individually to determine the weight and importance of the proportionality factors.

Through the years, many adjustments and additions to the proportionality factors have been added to "enable the court to keep tighter rein on the extent of discovery." Elizabeth D. Laporte & Jonathan M. Redgrave, *A Practical Guide to Achieving Proportionality Under New Federal Rule of Civil Procedure 26*, 9 FED. CT. REV. 20, 29 (2015) (citing Fed. R. Civ. P. 26, Advisory Committee Notes (1993)). The new changes to the Federal Rules of Civil Procedure emphasize that proportionality governs the scope of discovery.

Plaintiff makes many claims that the defendants failed to meet their burden on the proportionality analysis. But proportionality under Rule 26 is a two-way street. The burden of demonstrating the proportionality of the requested information is a collective responsibility between the parties and the court. Laporte & Redgrave at 40. A party requesting discovery must show how the requested information is important to the issues and resolution of the case: The responding parting must show the expense and burden responding. Id. The court can then balance the parties' interests and order discovery consistent with the proportionality mandated under the federal rules.

Although the parties in this case have both read and cited the law review article authored by Elizabeth D. Laporte & Jonathan M. Redgrave as an exemplary source, they make the same mistakes outlined in its text. They both take a fragmented and incomplete approach to the factors on which their individual burdens rest. And similar to the case of Maxtena Inc. v. Marks, 289 F.R.D. 427 (D. Md. 2012) cited within the article, the attorneys in this case put the onerous responsibility on the court to balance proportionality while failing to provide substantial and reasonable guidance on this key point: In its current state the court is being forced to "wade through generalized and conflated arguments of need, burden, and relevance." Laporte & Redgrave, at 50–51.

The court recognizes, and Plaintiff concedes, there is a substantial risk that responding to Plaintiff's discovery will be burdensome. (See Filing No. 82 at CM/ECF p. 15). But the extent of Defendant's burden has yet to be objectively quantified: Defendants have failed to submit affidavits or sworn information by employees or experts regarding the burden of searching for and providing information or providing any meaningful estimates for the time and cost required by the plaintiff's discovery.

Although the court has limited the current phase of discovery to the issue of whether Enbrel® can cause MDS, the parties have had significant disagreements regarding what this means. After all the briefings and hearings,[3] the court limits this phase of discovery as discussed below.

a. Limitations on Related Symptomology

The parties' disagreement centers on whether Plaintiff is entitled to studies and reports concerning a diagnosis of MDS, or of both MDS and all of its symptoms. Plaintiff requests all adverse event reports and Enbrel® studies linked to MDS and all related symptomology. MDS is not a specific disorder, but is a spectrum of disorders of the hematopoietic system affecting every blood cell type and the bone marrow. Due to its wide encompassing scale, Plaintiff argues that she should receive not only studies and reports related to and discussing "MDS," but also reports or studies discussing specific symptoms that may have actually indicated MDS even though the disease was not designated as such within the report or study.[4]

[3] Although the court has dedicated over five hours of conferencing time attempting to mediate the parties' discovery dispute, the plaintiff has made no concessions on the scope of her discovery demands, and the defendants have not quantified with any specificity the burden and expense of responding.

[4] Plaintiff's expert testified that having access to only the MedWatch adverse events reports on "MDS" and not the related symptoms would be only "the tip of the ice berg" and that "because the symptomology related to MDS is so serious, it's much more likely to be reported than MDS itself." (Filing No. 81 at CM/ECF p. 90). However, due to the great

The parties both look to the MedDRA's Standardized MedDRA Query ("SMQ") to determine the search terms. MedDRA is used by pharmaceutical companies as a dictionary and classification system for adverse effects. It was developed as a validated medical terminology for use throughout the regulatory process. Each MedDRA SMQ consists of a five-level hierarchy of terms which provides degrees or levels of superordination and subordination. The Low Level Terms ("LLTs") constitute the lowest level of the terminology and provides maximum specificity. Above each individual LLT, is an assigned Preferred Term ("PT"). PTs represent the primary level within the MedDRA SMQ and provide distinct descriptors for groups of similar LLTs.[5] After the PTs, the hierarchy advances as follows: High Level Terms ("HLTs"), High Level Group Terms ("HLGTs"), and finally, System Organ Classes ("SOCs"). Each LLT only fits in one place in the MedDRA hierarchy.[6]

Plaintiff requests reports and studies that mention every SMQ term as it may relate to MDS. However, the SMQ designates 206 LLTs for MDS. (See Filing No. 76-8 at CM/ECF pp. 1–9). Some of the LLTs are as general as anemia, fatigue, shortness of breath, pallor, unusual bruising, unusual bleeding, and frequent infections. Based on the great number of terms, the list of reports and studies for the defendants to produce could be great and many would not relate to MDS at all—especially if Defendants were forced to produce every report or study that mentioned terms as generic as "shortness of breath" or "fatigue." Plaintiff argues the search has to be broader than simply a search for "MDS," and repeatedly

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number of LLTs this "ice berg" is more likely a glacier. Many of the terms are so generic—i.e., parlor, shortness of breath, anemia—that the court does not find Dr. Levesque's rationale persuasive. If a doctor recognized the symptoms of MDS, the court believes that it would be labeled as such, and not reported as e.g., "shortness of breath."

[5] For example, the LLTs "Myelodysplasia syndrome transformative" and "Myelodysplasia syndrome classified" both belong under the PT "Myelodysplasic syndromes."

[6] For an example of the MedDRA terms, there are ~50,000 LLTs, ~18,000 PTs, ~3,000 HLTs, ~350 HLGTs, and 26 SOCs.

acknowledges that the court can enter an order narrowing the discovery search terms, but despite hours of hearings and hundreds of pages of briefing, offers no satisfactory or effective guideline for the court to whittle away at the 206 LLTs provided.

To prove his point on the ease of researching Plaintiff's discovery demands, during the December 9th hearing, Plaintiff's counsel ran a search of the adverse event reports submitted to the FDA based on Enbrel® as of September 30, 2011. This demonstration by Plaintiff's counsel proves the breadth of the plaintiff's discovery requests: The search retrieved 2,108 bone marrow failure reports; 684 aplastic anemia reports; 606 pancytopenia reports; 570 MDS reports; 64 marrow hyperplasia reports; 24 bone marrow disorder reports; and around 15 other terms with less than 20 adverse event reports. This search totaled approximately 4,193 adverse event reports[7] using 21 out of the 206 terms encompassed in the SMQ for MDS. And the courtroom search conducted retrieved only reports provided to the FDA, and not to other entities, and it included only the entry of a report—not the underlying research and follow up documentation as to each report.

Subsequent to the hearing, Defendants conducted a search of their global safety database for the "broad scope" of the SMQ terms. They identified 615 adverse event reports. They state, however, that the source documents for each report are not stored in the same location and would take significant effort to find. Defendants therefore argue the court should limit the search of terms to the "narrow scope" of the MDS SMQ. A search of their global safety database of the narrow scope identified 94 adverse event reports.[8]

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[7] (using an approximation of 15 reports for the 15 unnamed terms)

[8] Defendants claimed it took over 2 weeks for to procure results for the adverse event reports for the term "MDS" alone. Defendants state there is not one computer or database in which the terms can be entered and they search everything that Amgen and Wyeth and Pfizer have: It requires the systematic efforts of employee time and effort and money to go and run each of these searches. (Filing No. 81 at CM/ECF p. 95).

Most SMQs have both narrow and broad scope terms. (Filing No. 76-7 at CM/ECF p. 13). The narrow scope allows the user to search with specificity while a broad search allows for sensitivity. However, some SMQs have only narrow or broad terms. Examining the most recent SMQ Introductory Guide indicates that there is not a narrow or broad scope provided for MDS and Defendants do not indicate, nor can the court guess, how they gathered their terms to be used in the "narrow scope." (See Filing Nos. 76-7 & 76-8).

Nevertheless, the court finds the plaintiff's demands (as described by his expert) must be limited. After examining the MDS SMQ, the court orders that any discovery of adverse event reports and Enbrel® studies be limited to the Preferred Term "MDS" and its corresponding LLTs. This narrows the scope to the following 15 low level terms:

- Bone marrow dysplasia;
- Marrow Dysplasia;
- MDS;
- MDS transformation;
- Myelodysplasia;
- Myelodysplasia syndrome;
- Myelodysplasia syndrome NOS;
- Myelodysplasia syndrome transformative;
- Myelodysplasia syndrome unclassified;
- Myeloid dysplasia;
- Osteomyelodysplasia;
- Preleukaemia;
- Preleukemia;
- Refractory anaemia with excess blasts transformation; and
- Refractory anemia with excess blasts in transformation.

b. Reports on other TNF Blockers

Plaintiff requests "information on other TNF blockers." Plaintiff requests that the defendants 1) identify any study that it is aware of that relates any TNF blocker to MDS or

its symptoms; 2) determine if anyone associated with the defendants supplied any information for those studies; and 3) produce all such information.

Defendants object to this request on several grounds: They argue 1) the information is not relevant to causation because other TNF blockers do not use the same mechanisms and are prescribed for different conditions than Enbrel®; 2) this information is available in the public domain; 3) Defendants do not maintain a database on other TNF blockers produced and sold by other companies; and 4) any search by Defendants for this information would presumably require Defendants to search all files of Amgen's approximately 17,900 employees, Pfizer's approximately 78,300 employees, and the files of predecessor companies Immunex Corporation and Wyeth Inc.

Plaintiff retorts that this information is not in the public domain; is relevant because the drugs are routinely studied together and treated as a class by the FDA; and that the defendants could send a mass email to all of its employees seeking any pertinent information.

A party responding to discovery is not required to gather and produce documents that are publicly available. Nor are they required to produce items that are not in their custody or control. A discovery request which requires a party to email and search the files of close to 100,000 employees for information that may not exist and may have no relevancy whatsoever is unreasonable, and overbroad. For this reason, the court could simply sustain Defendant's objection. But the case is languishing. So the court will re-craft Plaintiff's discovery to match the case, and will order Defendants to answer or produce discovery regarding studies on the causal relationship, if any, between Enbrel® and MDS and produce such studies or reports within any Defendant's custody or control that are not available in the public domain.

c. Studies Involving All Indications

Enbrel® was administered to treat Decedent's psoriasis, but Plaintiff's discovery is not limited to that use of Enbrel®. Plaintiff seeks records on the use of Enbrel® for all types of diseases, disorders or symptoms. Defendants have agreed to produce documents and reports without regard to what Enbrel® was being used to treat, including the Biologic License Application ("BLA") for Enbrel®, and subject to the entry of a protective order, MedWatch reports, and the original Investigator's Brochure for Enbrel®. These documents, along with the documents produced as required under the remainder of this order, provide Plaintiff with the information needed to explore the existence of any causal connection between Enbrel® and MDS, while maintaining Defendants' burden proportionate to that need.

d. Custodial Information and Documents

Defendants have provided Plaintiff with the name of the one individual who has knowledge of the safety of Enbrel®, Ms. Jan Isles, who is the global safety officer in charge of Enbrel®. Defendants have also agreed to supplement the list of individuals with information as they become aware of them.

Plaintiff argues that the defendants should be ordered to provide the organizational charts of 1) the persons responsible for determining whether Enbrel® causes and/or is capable of causing MDS, and those working at their direction; 2) the person in charge of compiling adverse events, and those working at their direction; and 3) the person in charge of maintaining source documents for MDS adverse events. (See Filing No. 81 at CM/ECF p. 39).

During the December 9th hearing, the court ordered that given Enbrel®'s extensive history going back to the early 1990s and the fact that there were at least four companies involved with Enbrel®'s development and production since that time, Plaintiff's request is

overbroad and unreasonable. The plaintiff should instead depose Ms. Isles, and if she cannot provide the necessary information, Defendants may need to locate witnesses who can answer the plaintiff's relevant inquiries. (See Filing No. 81 at CM/ECF pp. 41–44).

CONCLUSION

In conclusion, the court will not require the defendants to provide discovery of every document in Defendant's possession that indicates a person who took Enbrel® was diagnosed as having a disease, disorder, or symptom commonly seen in people with low, or dysfunctional red cells, white cells, or platelets, or their precursor cells, whether in circulation or in the bone marrow. The court will not order a search for studies of the entire hematopoietic body system. Even without the defendants providing quantifiable evidence of burden, based on common sense and the search conducted by Plaintiff's counsel during the hearing, the court finds the burden of Plaintiff's discovery demands is unreasonable.

Given the tenor of the parties' discovery battles thus far, the court wants to make it clear that if any future discovery battles arise, the parties must provide the court a more thorough proportionality analysis with each side addressing and shouldering its burden: The party who served the discovery must show why the information is important to the issues and the party opposing discovery as overbroad must quantifiably explain the burden of providing the requested information. Absent such efforts by the parties, the court's future orders will not include judicial redrafting of discovery requests.

IT IS ORDERED:

1) On or before May 13, 2016, Defendants shall produce:

a. All adverse event reports and Enbrel® studies for the Preferred Term "MDS" and the following LLTs:

- Marrow Dysplasia;
- MDS;
- MDS transformation;
- Myelodysplasia;

- Myelodysplasia syndrome;
- Myelodysplasia syndrome NOS;
- Myelodysplasia syndrome transformative;
- Myelodysplasia syndrome unclassified;
- Myeloid dysplasia;
- Osteomyelodysplasia;
- Preleukaemia;
- Preleukemia;
- Refractory anaemia with excess blasts transformation; and
- Refractory anemia with excess blasts in transformation.

b. Produce documents regarding studies or reports on the causal relationship, if any, between Enbrel® and MDS and within any Defendant's control that are not available in the public domain.

c. The Biologic License Application ("BLA") for Enbrel®.

2) On or before April 11, 2016, the parties shall submit a jointly proposed protective order for the court's consideration.

3) Within 30 days after a protective order is entered for this case, Defendants shall produce MedWatch reports and the original Investigator's Brochure for Enbrel®.

4) On or before June 3, 2016, Ms. Jan Isles, the global safety officer in charge of Enbrel®, shall made available for a deposition to by conducted by Plaintiff's counsel.

5) A telephonic conference with the undersigned magistrate judge will be held on June 14, 2016 at 2:00 p.m. to discuss the status of case progression. The parties shall use the calling information assigned to this case, (see filing no. 66).

6) The clerk's office shall term Defendant's Analysis of Burdens. (Filing No. 80).

Dated this 28th day of March, 2016

BY THE COURT:

s/ Cheryl R. Zwart
United States Magistrate Judge